



Gemcabene Meets Primary Endpoint in INDIGO-1 Study of Severe Hypertriglyceridemia (SHTG) Patients

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Gemcabene demonstrated statistically significant lowering of triglycerides (TGs) in SHTG

Secondary endpoints achieved included statistically significant reductions in serum LDL-C, non-HDL-C, VLDL-C, apoB, apoE, apoCIII, and SAA

Gemcabene showed evidence of safety and tolerability in combination with statins

INDIGO-1 results further support Gemphire's rationale for developing gemcabene as a treatment for NAFLD/NASH

Conference call and webcast today, Thursday, June 28, at 4:30 p.m. Eastern Time

LIVONIA, Mich., June 28, 2018 (GLOBE NEWSWIRE) -- Gemphire Therapeutics Inc. (NASDAQ:GEMP), a clinical-stage biopharmaceutical company focused on developing and commercializing therapies for cardiometabolic disorders, including dyslipidemia and nonalcoholic steatohepatitis (NASH), today announced that it achieved the primary endpoint, reduction of TGs by gemcabene, in its Phase 2b INDIGO-1 trial in SHTG patients with baseline serum TGs >500 mg/dL.

Key findings:

- Primary endpoint met with median TGs significantly decreased by 47% in gemcabene (600 mg) treated patients compared to 27% for placebo-treated patients (P=0.0063; ranked ANCOVA).
- The 600 mg gemcabene group attained a significantly lower median level of serum TGs of 333 mg/dL compared to placebo of 538 mg/dL (P=0.0137) at the end of the study.
- Statistically significant secondary endpoints achieved with 600 mg gemcabene, including placebo-corrected median decreases in LDL-C (24%), non-HDL-C (16%), VLDL-C (19%), apoB (12%), apoE (14%), apoCIII (11%), SAA (23%); (p-values <0.05; ranked ANCOVA).
- No severe adverse events (SAEs) were observed with gemcabene and adverse events (AEs), which were generally mild to moderate, occurred less frequently with gemcabene than placebo.

"We are pleased to reach this milestone of meeting both primary and multiple secondary endpoints and look forward to advancing gemcabene into Phase 3 trials," said Dr. Steven Gullans, CEO of Gemphire. "There are approximately 3.5 million SHTG patients in the United States in need of lowering their TG levels below 500 mg/dL to reduce their risk of developing acute pancreatitis. Our once daily tablet has demonstrated promising evidence of safety, efficacy and tolerability in more than 1,100 subjects thus far. Moreover, in prior studies 600 mg of gemcabene reduced LDL-C, hsCRP and other biomarkers that are typically elevated in a broad range of dyslipidemic conditions."

INDIGO-1 was designed as a dose-ranging, 12 week, multicenter, double-blind, placebo-controlled, randomized trial in patients with SHTG (TG ≥500 mg/dL and < 1500 mg/dL) with or without background statin therapy. All patients enrolled in the study were also counseled on the importance of maintaining a heart-healthy diet and limiting alcohol intake. Patients were enrolled into one of three arms: gemcabene 300 mg (n=30), gemcabene 600 mg (n=30) or placebo (n=31) once daily. Demographically the 3 groups were comparable: ~40% diabetic, 50% on statin therapy, median Body Mass Index (BMI) ~31-32, and mean age of 54; one group difference was a larger proportion of females in the placebo group (39%) compared to the gemcabene groups (300 mg: 3%; 600 mg: 17%). The primary endpoint was median percent change in TGs from baseline to the end of study (defined as the average of weeks 10 and 12). Other endpoints associated with atherogenic burden included percent changes in LDL-C, hsCRP, apoB, non-HDL-C, very-low-density lipoprotein cholesterol (VLDL-C) and total cholesterol.

People with TG levels above 500 mg/dL are at increased risk for acute pancreatitis, a very serious and potentially lethal complication of SHTG, and therefore, this study focused only on SHTG patients. Starting from a median TG baseline of 637 mg/dL, patients receiving 600 mg of gemcabene experienced a median 47% decrease in TGs compared to a median 27% decrease for placebo patients, who started at a median of 658 mg/dL (P=0.0063; ranked ANCOVA). Once daily 600 mg of gemcabene decreased median TG levels more than 300 mg of gemcabene.

Importantly, since the goal of treating SHTG patients is to reduce TGs below 500 mg/dL, the absolute levels of TGs were evaluated in the trial. Gemcabene 600 mg treatment reduced median TG levels from a baseline of 637 mg/dL to 333 mg/dL, compared to placebo treated patients with a median baseline of 658 mg/dL reduced to 538 mg/dL (P=0.0137). In addition, 67% of these 600 mg gemcabene treated patients achieved a serum TG level below 500 mg/dL and some patients experienced more than a 70% reduction from baseline.

Cardiometabolic patients, including those with SHTG, often have high levels of serum lipid and inflammatory biomarkers. In the 600 mg gemcabene

cohort, multiple secondary endpoints were achieved. In particular statistically significant placebo-corrected percent decreases were observed for serum LDL-C (24%), non-HDL-C (16%), VLDL-C (19%), apoB (12%), apoE (14%), apoCIII (11%), and SAA (23%); (p-values <0.05; ranked ANCOVA). A placebo-corrected 26% decrease in serum hsCRP was observed but this did not achieve statistical significance (P<0.08).

With regard to safety, gemcabene appeared safe and well-tolerated as monotherapy or as add-on to statins. Overall, gemcabene patients experienced mild to moderate AEs whose frequency was less than that observed with the placebo group. One placebo patient had an SAE, while there were no SAEs in gemcabene patients. There were no withdrawals due to AEs. One patient with an elevated alanine transaminase (ALT) at baseline experienced a confirmed, repeat value for ALT > 3 x upper limits of normal on 600 mg of gemcabene, which, importantly, spontaneously resolved while remaining on active treatment.

Patients with mixed dyslipidemia (defined as LDL-C ≥100 mg/dL and TGs ≥ 200 mg/dL) are a particularly high risk subset of patients including many with SHTG. An analysis of this small subset of patients (n=9 for placebo; n=14 for gemcabene 600mg) in INDIGO-1 showed directional and/or significant reductions in placebo-corrected median TGs of 30% (p=0.1289), LDL-C of 28% (p=0.0012), non-HDL-C of 38% (p=0.0002), VLDL-C of 61% (p=0.0398) apoB of 28% (p=0.0023), apoE of 43% (p=0.0009), apoCIII of 27% (p=0.1356), hsCRP of 48% (p=0.1554), and SAA of 37% (p=0.1823); all p-values from ranked ANCOVA.

"The INDIGO-1 phase 2 study in severe hypertriglyceridemia clearly shows the 600 mg dose of gemcabene to be effective and well tolerated in this difficult to treat population," stated Dr. Evan Stein, Director Emeritus, Metabolic & Atherosclerosis Research Center, Cincinnati. "Importantly the triglyceride reduction is well supported by significant reductions in LDL-C, apoB, apoE, and apoCIII and these potentially beneficial reductions were greater in the subgroups that are even more difficult to treat, those with diabetes and already on statins."

In keeping with the Company's ongoing clinical trial plans, the INDIGO-1 results further support Gemphire's rationale for pursuing gemcabene to treat NAFLD/NASH. Patients in the present study had profiles typical of cardiometabolic patients who often suffer from diabetes, dyslipidemia and obesity, which puts them at high risk for NAFLD/NASH. NAFLD may be present in up to 90% of all obese persons and up to 70% of Type-II diabetic patients. NAFLD/NASH patients typically present with an atherogenic dyslipidemic profile, characterized by increased serum levels of TGs, apoB, VLDL-C, and LDL-C with a proportionally greater content of small dense LDL-C (sdLDL-C) (Clin Gastroenterol Hepatol 2015;13:1000; Diabetes Metab Syndr 2016;10(2 Suppl 1):S77; Metabolism 2016;65:1109). NAFLD is also associated with aberrant nuclear receptor function and systemic inflammation. (Biochim Biophys Acta. 2016;1859:1083). The promising evidence that Gemcabene can improve the dyslipidemic and inflammatory profile of cardiometabolic patients, suggests that it could provide benefit for NAFLD/NASH.

In prior studies, gemcabene reduced serum levels of TGs, LDL-C, VLDL-C, apoB and hsCRP in hypercholesterolemic and hyperlipidemic patients. Additionally, in animal and cell based models, gemcabene demonstrates a reduction in *de-novo* lipogenesis, modulation of inflammation and reduction of the NAFLD activity score (NAS), particularly related to hepatic ballooning, steatosis, fibrosis, and collagen accumulation. Accordingly, in 2018 Gemphire initiated proof-of-concept trials in pediatric NAFLD and adult familial partial lipodystrophy. The results of the subgroup analysis in mixed dyslipidemic patients in INDIGO-1 reaffirms previous clinical data in patients at high risk for having NAFLD/NASH.

"The ability to reduce TGs in patients with SHTG, who are at risk of developing pancreatitis, to below 500 mg/dL is an important goal of therapy in this high risk patient group," added Dr. Lee Golden, Chief Medical Officer of Gemphire. "In patients treated with gemcabene 600 mg, 67% of patients achieved this goal. Gemcabene continues to demonstrate reductions in the overall atherogenic particle burden as well as inflammatory biomarkers. In particular, cardiometabolic patients, including mixed dyslipidemic patients, who often have NAFLD/NASH as well, showed greater reductions in lipid and inflammatory parameters."

"On a related note, we are pleased to report that both of our ongoing NAFLD/NASH proof-of-concept trials are dosing patients and remain on track to report data in late 2018 and early 2019 as previously guided," continued Dr. Golden. "In addition, we are using the information from our INDIGO-1 trial, particularly the dose finding results, together with the results from our previous Phase 1 and 2 clinical trials, to finalize our Phase 3 trial plans. We expect to communicate more information regarding the structure and timing of our Phase 3 program once we have completed our End of Phase 2 meeting with the FDA, which we will request following the completion of the FDA's review of the 2-year carcinogenicity study, which is currently in progress."

Conference Call and Webcast

The Company will host a conference call and webcast today Thursday, June 28, at 4:30 pm Eastern Time. To access the audio conference, please dial (844) 494-0188 (domestic) or +1 (425) 278-9114 (international) and reference conference ID 4998205. To view the slides, please see the News & Events section of the Gemphire website. The live webcast can be accessed via the following link: <https://edge.media-server.com/m6/p/r8uwpgpi>. A webcast replay will be available on the News & Events section of the Gemphire website for all interested parties following the call and will be archived and available for 90 days.

About Severe Hypertriglyceridemia (SHTG)

SHTG is a condition in which patients have TGs present in the bloodstream at a level of greater than 500 mg/dL. High TG levels are associated with an increase in both the risk for cardiovascular disease and acute pancreatitis. As high TG can lead to organ failure which can be life-threatening, the current first-line treatments for SHTG, as recommended by the ATP III guidelines, include dietary modifications to lower the intake of fatty foods and the use of fibrates, prescription fish oils and/or niacin. Current therapies, limited by insufficient efficacy, drug-drug interaction potential or side-effects, may be inadequate to lower the TG levels below 500 mg/dL, the level at which patients are at risk for increased pancreatitis.

Pursuing SHTG may enable gemcabene to reach a large population of patients with TG levels above 500 mg/dL and offer an oral, once-daily dosing with no observed food effects that may have the potential to offer improved efficacy than standard of care, while being used concomitantly with statins. Based on a 1.1% prevalence rate of TG ≥ 500mg/dL in the United States, as published by the American Heart Association, Gemphire estimates there are approximately 3.5 million patients with SHTG in the United States and 75 million patients in the rest of the world, at risk for developing acute pancreatitis.

About Pancreatitis

Pancreatitis is an inflammation of the pancreas. Once the gland becomes inflamed, the condition can progress to swelling of the gland and surrounding blood vessels, bleeding, infection, and damage to the gland. Digestive juices become trapped and start digesting the pancreas itself. If the damage persists, the gland may not be able to carry out normal functions. Pancreatitis may be acute (new, short-term) or chronic (ongoing, long-term). Either type can be very severe, and lead to serious complications.

Acute pancreatitis usually begins soon after the damage to the pancreas begins. Attacks are typically very mild. Mild attacks may last for a short time and usually resolve completely as the pancreas returns to normal. Some people only have one attack, whereas other people may have more than one attack. About 20% of cases, however, are very severe. Chronic pancreatitis begins as acute pancreatitis. If the pancreas becomes scarred during the attack of acute pancreatitis, it cannot return to its normal state. The damage to the gland continues, worsening over time. There are reports that more than 300,000 patients are admitted per year for pancreatitis in the United States, and about 20,000 of those patients die from the disease. Pancreatitis can occur in people of all ages, although it is very rare in children. Pancreatitis occurs in men and women, although chronic pancreatitis is more common in men.

High levels of TGs are associated with acute pancreatitis and considerable morbidity and mortality. In September 2002, the National Institutes of Health (NIH) published its Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Although the focus of the report is on LDL-cholesterol and HDL-cholesterol levels, it also provides guidance for treatment of patients with high TG levels. The report states that in cases in which a person's TGs are very high (≥ 500 mg/dL), the initial aim of therapy is to prevent acute pancreatitis through triglyceride lowering.

Gemcabene's mechanism of action and safety profile are highly differentiated from other clinical candidates

Gemphire's product candidate gemcabene is a first-in-class, once-daily, oral therapy that may be suitable for patients who are unable to achieve normal levels of LDL-C or TGs with currently approved therapies, primarily statins. Gemcabene's mechanism of action (MOA) enhances the clearance of very low-density lipoproteins (VLDLs) in the plasma and inhibition of the production of cholesterol and TGs in the liver. The combined effect of these mechanisms has been clinically observed to result in a reduction of plasma non-HDL-C, VLDL-C, LDL-C, apolipoprotein B and TGs. In addition, gemcabene has been shown to markedly lower C-reactive protein in humans and improve insulin sensitization. Gemcabene's MOA is liver-directed involving downregulation of hepatic apolipoprotein C-III (apoC-III) mRNA expression and decrease of plasma apoC-III levels. Gemcabene has also been shown to reduce liver sulfatase-2 mRNA levels, known to be elevated in diabetic and obese patients. Elevated sulfatase-2 is thought to reduce the effectiveness of the liver VLDL-remnant receptor (also known as Syndecan-1), that normally plays a role in removing TG containing particles from the plasma. Gemcabene also reduces acetyl-CoA carboxylase (ACC1) and CCR2/CCR5 receptor mRNA levels, markers involved in the progression of NASH/NAFLD. Gemcabene has demonstrated POC efficacy for NASH in the rodent STAM™ model developed at SMC Laboratories in Tokyo, Japan. Gemcabene has been tested as monotherapy and in combination with statins and other drugs in nearly 1,200 subjects across 25 Phase 1 and Phase 2 clinical trials. Given this profile of efficacy across multiple pathological pathways, as well as evidence of safety and tolerability, particularly when used as an add-on to many other therapeutic drugs, gemcabene has attributes that support studies in humans for NASH.

About Gemphire

Gemphire is a clinical-stage biopharmaceutical company that is committed to helping patients with cardiometabolic disorders, including dyslipidemia and NASH. The Company is focused on providing new treatment options for cardiometabolic diseases through its complementary, convenient, cost-effective product candidate gemcabene as add-on to the standard of care, especially statins that will benefit patients, physicians, and payors. Gemphire's Phase 2 clinical program is evaluating the efficacy and safety of gemcabene in hypercholesterolemia, including FH and ASCVD, SHTG and NASH/NAFLD. Two trials supporting hypercholesterolemia and one trial in SHTG have been completed under NCT02722408, NCT02634151 and NCT02944383, respectively, and the Company has initiated two proof-of-concept trials for NAFLD/NASH. Please visit www.gemphire.com for more information.

Forward Looking Statements

Any statements in this press release about Gemphire's future expectations, milestones, goals, plans and prospects, including statements about Gemphire's financial prospects, future operations and sufficiency of funds for future operations, clinical development of Gemphire's product candidate, expectations regarding future clinical trials, regulatory submissions and meetings and future expectations and plans and prospects for gemcabene, expectations for the future competitive environment for gemcabene, expectations regarding operating expenses and cash used in operations, and other statements containing the words "believes," "anticipates," "estimates," "expects," "intends," "plans," "predicts," "projects," "promising," "targets," "may," "potential," "will," "would," "could," "should," "continue," "scheduled" and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: developments in the capital markets, the success and timing of Gemphire's regulatory submissions and pre-clinical and clinical trials; regulatory requirements or developments; changes to Gemphire's clinical trial designs and regulatory pathways; changes in Gemphire's capital resource requirements; the actions of Gemphire's competitors; Gemphire's ability to obtain additional financing; Gemphire's ability to successfully market and distribute its product candidate, if approved; Gemphire's ability to obtain and maintain its intellectual property protection; and other factors discussed in the "Risk Factors" section of Gemphire's annual report and in other filings Gemphire makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent Gemphire's views as of the date hereof. Gemphire anticipates that subsequent events and developments will cause Gemphire's views to change. However, while Gemphire may elect to update these forward-looking statements at some point in the future, Gemphire specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing Gemphire's views as of any date subsequent to the date hereof.

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